

By way of antedating Boyce et al., applicants submit herewith the Declaration of Todd M. Boyce pursuant to 37 C.F.R. § 1.131 (the "Boyce Declaration"). As stated in the Boyce Declaration, Boyce et al. issued on May 4, 1999 on original application Serial No. 09/009,997 filed on January 21, 1998. The subject application was filed on April 5, 2000 as a continuation of U.S. patent application Serial No. 09/020,205 filed February 6, 1998. As established by the Boyce Declaration and accompanying documentary exhibit, the invention claimed herein was completed prior to the January 21, 1998 filing date of the application underlying the grant of the Boyce et al. patent. Accordingly, Claims 1-7, 9-21, 23-43, 45-61, 63-80 and 82-134 are not anticipated by Boyce et al. Moreover, as Claims 95-134 were rejected on no ground other than on anticipation over Boyce et al., applicants respectfully submit that Claims 95-134 are in condition for immediate allowance, formal notice thereof by the Examiner being respectfully requested.

The Examiner has maintained the rejection of Claims 1-7, 9-11, 13, 14, 19-21, 23, 34-43, 45, 56-61, 63, 74-80, 82 and 93-94 under 35 U.S.C. §102(b) as anticipated by Lyle U.S. Patent No. 5,061,286 ("Lyle"). According to the Examiner, Lyle discloses demineralized bone particles (which, of course, possess surface-exposed collagen) that are "linked together" with a binder such as cyanoacrylate. The Examiner asserts: "In response to the traversal of the Lyle 35 USC 102(b) rejection that Lyle does not teach binding of particles to each other, the Examiner posits that the cement of[sic] adhesive of Lyle provides the chemical linkages to bind the particles together."

(October 23, 2003 Office Action at page 5.)

While the Lyle demineralized bone particles possess surface-exposed collagen, there is not the slightest hint anywhere in this disclosure of the demineralized bone particles being "bonded to each other through chemical linkages *between their surface-exposed collagen*". Contrary to the Examiner's assertion, Lyle's cement or adhesive component does not form or provide *chemical linkages* between the surface-exposed collagen of adjacent bone-derived elements as in the osteoimplant of applicants' claims but applies demineralized bone particles to the surface of a prosthetic device by means of a material that functions as an adhesive or cement, specifically, a cyanoacrylate. Cyanoacrylates work as adhesives when they undergo curing, which is to say, polymerization, to form a polymer. Cyanoacrylates do provide chemical bonds but those bonds are formed between monomeric units of cyanoacrylate to provide the polymeric adhesive. The chemical bonds that form during the curing of the cyanoacrylate do *not* form between surface exposed collagen of the Lyle demineralized bone particles but, as said, between units of cyanoacrylate monomer. There is nothing in Lyle or in the literature of cyanoacrylate adhesives to indicate otherwise. See, e.g., Courtney et al., "Advances in Cyanoacrylate Technology for Device Assembly", Medical Device & Diagnostic Industry, September, 1999, available on the Internet at <http://www.devicelink.com/mddi/archive/99/09/006.html>; Schwade, N.D., "Wound Adhesives, 2-Octyl Cyanoacrylate" eMedicine, April 10, 2002, available on the Internet at <http://www.emedicine.com/ent/topic375.htm> (copies of which are attached hereto for the Examiner's convenience).

One skilled in the art reviewing Lyle would clearly recognize that cyanoacrylate adhesives as disclosed therein differ from applicants' claimed invention wherein individual bone elements are "bonded to each other through chemical linkages between their surface-exposed collagen". In lacking any disclosure or suggestion of such chemical linkages, Lyle fails to anticipate or render obvious the subject matter of any of Claims 1-7, 9-11, 13, 14, 19-21, 23, 34-43, 45, 56-61, 63, 74-80, 82 and 93-94.

The Examiner has maintained the rejection of Claims 11-14, 16, 19-21, and 34-35 under 35 U.S.C. §102(b) for anticipation by Jefferies U.S. Patent No. 4,394,370 ("Jefferies").

According to the Examiner, Jefferies discloses demineralized bone particles whose surface-exposed collagen is crosslinked, thereby inherently improving the mechanical strength of the resulting product. In response to applicants' prior arguments, the Examiner states as follows (October 23, 2003 Office Action at page 5):

Applicants traverse the Jefferies 35 USC 102(b) rejection by arguing that it does not disclose reinforcing particles or fillers. However, the Examiner posits that at least collagen is the filler material. In addition, Example III discloses another filler in the form of macromolecules. These materials are fillers to the extent that such a term can be given patentable weight.

Applicants argue that Jefferies lacks the claimed compression strength as set forth in claim 1. However, the rejection of claim 1 and its dependent claims has been withdrawn. This argument is not relevant all[sic] but a few of the other claims.

Finally, Applicants traverse Jefferies by stating that there is no reinforcement component therein. However, the claims only require reinforcing particles. The filler need not have a reinforcing function. Nonetheless, the filler of Jefferies (i.e. collagen or macromolecules) provide reinforcement by serving as vehicles for chemical bonding.

According to the foregoing passage, the Examiner has withdrawn the rejection of Claim 1 and the claims dependent thereon as anticipated by Jefferies. Since rejected Claims 11-14, 16, 19-21 and 34-35 depend from Claim 1, it follows that this rejection was inadvertently made. If this is not the case, applicants would appreciate a clarification from the Examiner.

Claims 11-14, 16, 19-21 and 34-35 recite that where *substantially all* of the bone-derived elements are substantially completely demineralized bone-derived elements, the osteoimplant contains at least one additional component selected from the group consisting of reinforcing particles and fillers, such that the solid aggregate of bone-derived elements possesses a compression strength of from about 10 to about 200 MPa.

Contrary to the Examiner's assertion, the collagen or macromolecules (which are, in fact, enzymes) of Jefferies cannot properly be considered a filler, as the purpose of these components in the Jefferies graft is either the formation of a sponge (when collagen is used) and the modification or acceleration of the osteogenic properties of the materials (when the macromolecules are added). Moreover, Jefferies' recitation of collagen, in addition to the demineralized bone particles, is redundant as demineralized bone particles are, in essence, collagen. Accordingly, contrary to the Examiner's assertion, neither of these components may properly be considered the separate filler of applicants' invention as neither will provide the compression strength of applicants' osteoimplant.

Jefferies also lacks any suggestion of incorporating a reinforcing component of any kind into the grafting implant. The Jefferies demineralized bone particles are

substantially completely demineralized bone particles, i.e., they contain little if any of their original mineral content, primarily made up of calcium compounds. Neither the collagen nor the macromolecules (enzymes) of Jefferies would improve the mechanical properties of the aggregated demineralized bone particles as the reinforcing particles of applicants' invention. In fact, the Examiner ignores the fact that Jefferies' grafting implant is described as a sponge, which possesses a majority, i.e., more than 50 weight percent collagen, and is not intended to be used in circumstances where it can be expected to sustain relatively high mechanical loads. Thus, at column 2, lines 39-45, Jefferies discloses that implants according to the invention (referred to in the cited passage as "complexes") can be made into "thin membranes", "gels" or "preferably in a sponge-like configuration". These final products by their very nature are not intended to withstand high mechanical stresses. This being the case, the Jefferies grafting implant lacks any significant mineral content that would elevate its mechanical strength beyond that of the aggregated demineralized bone particles themselves.

In contrast to Jefferies' products, applicants' osteoimplant must possess some component which, in effect, imparts mechanical strength to crosslinked bone elements which is above and beyond that of merely crosslinked substantially completely demineralized bone elements. This mechanical strength-supporting component can be provided by the mineral content of superficially demineralized bone-derived elements (when such are employed) or when such mineral content is absent, or nearly absent, some added reinforcing particles/fillers. Due to this arrangement, applicants' osteoimplant can be used to repair or replace a variety of bones where mechanical

strength of the osteoimplant is a practical consideration, as the solid aggregate of bone-derived elements which make up the osteoimplant possess a compression strength of from about 10 to about 200 MPa. (See, e.g., the disclosure at pages 13 and 14 of the specification.)

In view of the foregoing, Claims 11-14, 16, 19-21, and 34-35 are both novel and nonobvious over the Jefferies disclosure.

The Examiner has maintained the rejection of Claims 12 and 15-18 under 35 U.S.C. §103(a) for obviousness over Lyle. The Examiner characterizes Lyle's "cyanoacrylate" as a crosslinking agent. However, as noted above in connection with the Examiner's rejection of the claims for supposed anticipation by Lyle, cyanoacrylate is a monomer which provides a polymer, the polymer being the actual adhesive which binds the Lyle demineralized bone particles together. There is no disclosure or suggestion in Lyle that cyanoacrylate functions in any other way.

In the absence of any indication in Lyle that the demineralized bone particles therein are bonded to each other through chemical bonds formed in their collagen-exposed surfaces, Claims 12 and 15-18 can only be regarded as nonobvious, and therefore patentable, over Lyle.

In view of the foregoing remarks, reconsideration and allowance of all the claims of the application, i.e. Claims 1-7, 9-21, 23-43, 45-61, 63-80 and 82-134, are respectfully requested.

Respectfully submitted,

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